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Central versus Local Radiological Reading of Acute Computed Tomography Characteristics in Multi-Center Traumatic Brain Injury Research

Thijs Vande Vyvere,[1] Guido Wilms,[2,3] Lene Claes,[2] Francisco Martin Leon,[2] Daan Nieboer,[4] Jan Verheyden,[2] Luc van den Hauwe,[1,2] Pim Pullens,[6] Andrew I.R. Maas,[5] Paul M. Parizel[1]
and the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) Investigators and Participants*

Abstract

Observer variability in local radiological reading is a major concern in large-scale multi-center traumatic brain injury (TBI) studies. A central review process has been advocated to minimize this variability. The aim of this study is to compare central with local reading of TBI imaging datasets and to investigate the added value of central review. A total of 2050 admission computed tomography (CT) scans from subjects enrolled in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study were analyzed for seven main CT characteristics. Kappa statistics were used to calculate agreement between central and local evaluations and a center-specific analysis was performed. The McNemar test was used to detect whether discordances were significant. Central interobserver and intra-observer agreement was calculated in a subset of patients. Good agreement was found between central and local assessment for the presence or absence of structural pathology (CT+, CT–, $\kappa=0.73$) and most CT characteristics ($\kappa=0.62$ to 0.71), except for traumatic axonal injury lesions ($\kappa=0.37$). Despite good kappa values, discordances were significant in four of seven CT characteristics (i.e., midline shift, contusion, traumatic subarachnoid hemorrhage, and cisternal compression; $p=0.0005$). Central reviewers showed substantial to excellent interobserver and intra-observer agreement ($\kappa=0.73$ to $\kappa=0.96$), contrasted by considerable variability in local radiological reading. Compared with local evaluation, a central review process offers a more consistent radiological reading of acute CT characteristics in TBI. It generates reliable, reproducible data and should be recommended for use in multi-center TBI studies.

Keywords: agreement; central radiology review; traumatic brain injury

Introduction

Computed tomography (CT) imaging remains the modality of choice for assessing structural brain damage in the acute phase after traumatic brain injury (TBI).[1–3] It allows for the detection of most injuries and can indicate the need for surgical intervention or intracranial pressure management.[1,4]

Several acute CT characteristics and intracranial lesion types have shown to be strong predictors of clinical outcome.[5–9] In large-scale multi-center research initiatives, they are therefore often collected and assessed by investigators as key radiological variables.[10,11] However, the investigator-based assessment process is taking place in an acute clinical setting, which is difficult to standardize. Depending on the number of participating clinical centers, the pool of readers can become very heterogeneous in terms of experience, training, and use of terminology. This has been associated with high observer variability and can possibly confound statistical analyses.[12,13]

Various reports have stressed the importance of minimizing observer variability and have advocated a centralized reading process.[12,14] In central review, a limited pool of independent readers, blinded to patient information, receive uniform training to assess images according to a standardized reading protocol.[13] A standard lexicon of common data elements (CDEs) is used that can be entered into structured templates.[15] This approach to evaluation already has shown great benefits in other fields of medicine.[13] Not only can it

[1]Department of Radiology, [5]Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium.
[2]icometrix, Research and Development, Leuven, Belgium.
[3]Department of Radiology, University Hospital Leuven and Catholic University of Leuven, Leuven, Belgium.
[4]Department of Public Health, Erasmus University Rotterdam, Rotterdam, the Netherlands.
[6]Department of Radiology, Ghent University Hospital, Ghent, Belgium.
*CENTER-TBI investigators and participants listed at end of the article.

minimize observer variability, but it can also provide highly structured data that may facilitate cohort analysis of large datasets across and between different TBI studies.[10]

Despite the implementation of both radiological reading approaches in multi-center TBI research projects, the degree of agreement between central and local assessments has not been extensively studied. Our objective was therefore to determine the value of a central reading process by comparing central and local assessments of acute CT characteristics, by computing central interobserver and intra-observer agreement and by investigating the variability of local radiological readings.

Methods

Study population and CT assessors

This study was conducted in the context of the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI)[10] project, that included a multi-center longitudinal and observational study (registered at clinicaltrials.gov: NCT02210221). The CENTER-TBI study implemented both central and local reading of CT characteristics. Patients with a clinical diagnosis of TBI and an indication for CT scanning were enrolled in three strata, differentiated by care path: Emergency Room (ER) stratum (patients discharged from the ER), Admission (ADM) stratum (patients admitted to the hospital ward), or Intensive Care Unit (ICI) stratum (patients admitted primarily to the ICU). The study protocol was approved by the national and local ethics committees for each participating center. Informed consent, including use of data for other research purposes, was obtained in each subject according to local regulations.

For this study, we used data on 2050 CT scans, obtained between January 2015 and March 2018, from 34 centers that enrolled at least 10 patients. Imaging datasets that had been labeled as ''uninterpretable'' by the central reviewers (i.e., datasets with large artefacts or noise) were excluded from the analysis. At minimum, transverse scans with reconstructed section thickness of 3–5 mm were present in all datasets. All centers used routine clinical protocols. CT scanners came from four different vendors (i.e., Siemens, 16 centers; General Electric, eight centers; Philips, five centers; and Toshiba, five centers). The majority of scanners were 64 slice-dual source (65%) or 128 slice-dual source (24%) CT scanners. Only four centers (12%) were 16 slice dual source.

Initial radiological assessments were performed by local radiologists, radiology residents, neurosurgeons or intensivists according to their own local clinical practices. Findings were entered into a clinical database via electronic case report forms by either the physician who performed the assessment (15/34 centers) or by a third person (19/34 centers), based on the radiological report. CT scans were then de-identified and transferred to a central imaging repository for storage and independent central reading. Patients were coded by means of a Global Unique Patient Identifier to ensure adequate de-identification. The central review panel consisted of three protocol-trained reviewers (i.e., one supervising neuroradiologist with over 25 years of clinical experience at the time of the study, and two neuroanatomists, trained to read head CTs for the CENTER-TBI study with 1 to 2 years of experience at the time of the study) who entered CT characteristics into custom-made structured templates, according to the National Institute of Neurological Disorders and Stroke (NINDS) TBI Common Data Elements (TBI-CDE).[15] These are standardized formats with common terminology and operational definitions to interpret radiologic images of TBI patients. The reviewers were blinded to local assessment and clinical patient information, except for gender, age, and care path stratum. Each CT report was generated by consensus between one of the two neuroanatomists and the expert neuroradiologist.

Observer agreement

Agreement between central and local assessments. The following overlapping seven acute CT characteristics were extracted from the 2050 assessments in the clinical database and the central imaging repository: epidural hematoma, subdural hematoma, traumatic subarachnoid hemorrhage (tSAH), contusion, traumatic axonal injury (TAI), midline shift (MLS), and cisternal compression. For the purposes of this study, we defined a positive CT scan (CT+) as a CT scan showing any of the selected CT characteristics. A negative CT scan (CT−) was defined as a CT scan showing none of the selected CT characteristics. The dataset consisted of 1364 males (67%) and 686 females (33%) with a median age of 51 years (standard deviation [SD] = 21.99). A total of 451 (22%) patients were in the ER stratum, 716 (35%) patients were in the admission stratum, and 883 (43%) were in the ICU stratum. Scans came from 34 clinical centers in Europe, with a minimum of 11 and a maximum of 234 scans per center.

Variability between centers in agreement with central review. For the center-specific analysis, we calculated the agreement between the individual centers and the central review and retrospectively sent out a questionnaire to the participating centers to estimate the number of readers that were involved in initial CT assessment and to disclose the background and experience of the local readers.

Agreement between central reviewers. A subset of 100 unread CT examinations was randomly selected from the imaging repository and independently assessed by the three central reviewers to calculate interobserver agreement. This smaller dataset consisted of 69 males (69%) and 31 females (31%), with a median age of 49.5 years (SD = 18.64). A total of 22 were ER patients (22%), 29 were admitted to the hospital (ADM; 29%) and 49 patients were ICU patients (49%). Scans came from 20 centers in Europe, with a minimum of one and a maximum of 16 scans per center. A consensus dataset was created based on the readings of the three reviewers and used to compare with the lesions reported by the centers in the larger dataset. We performed this analysis to ensure that the smaller sample ($n = 100$) was representative of the larger sample ($n = 2050$). The presence of CT characteristics did not statistically differ from the larger dataset ($n = 2050$) for five of seven characteristics (CT+, contusion, tSAH, MLS, and TAI; $p > 0.005$). Two characteristics were more prevalent in the smaller dataset: basal cistern compression and acute subdural hematoma (22% vs. 11%, $p = 0.002$; and 44% vs. 28%, $p = 0.001$). These findings indicate that the two datasets had a similar overall composition, with slightly more pathology in the smaller dataset. Intra-observer agreement was calculated on a subset of 20 CT scans that were randomly drawn from the smaller data set ($n = 100$) and were assessed by each central reviewer a second time, with a minimum interval of 4 months between reviews.

Statistical analysis

Cohen's kappa statistics were calculated to assess the overall agreement between central and local assessments and to assess the intra-observer agreement between central reviewers. Fleiss' kappa statistics were used to calculate interobserver agreement between the three central reviewers. Values below 0.2 indicate poor agreement; between 0.21 and 0.4, fair agreement; between 0.41 and 0.60, moderate agreement; between 0.61 and 0.8, substantial agreement; and >0.8, excellent agreement.[16]

For each individual CT characteristic, we calculated the McNemar's test to determine if the differences in the proportion of discordant findings between central and local readings were significant, taking into account the matched data.[17] As opposed to Cohen's kappa, the McNemar test only takes into account the

Table 1. Agreement between Central and Local Radiological Evaluation of 2050 Admission CT Scans

	Central and site agreement (n = *2050*)	*Detection frequency*		*Concordance* (n)		*Discordance* (n)		*McNemar*
	Kappa (95% CI)	*Central* (n)	*Site* (n)	+/+	–/–	+/–	–/+	(p *value)*
CT+	0.73 (0.70–0.76)	1221 (60%)	1222 (60%)	1098	696	133	132	1.000
CT–	0.73 (0.70–0.76)	829 (40%)	828 (40%)	696	1098	132	133	1.000
Epidural hematoma	0.64 (0.59–0.70)	221 (11%)	217 (11%)	149	1761	72	68	0.800
Acute subdural hematoma	0.63 (0.59–0.67)	574 (28%)	587 (29%)	425	1315	148	162	0.460
tSAH	0.65 (0.62–0.68)	931 (45%)	770 (38%)	677	1026	254	93	0.000
Contusion	0.62 (0.58–0.65)	603 (30%)	692 (34%)	477	1232	126	215	0.000
TAI	0.37 (0.31–0.44)	188 (9%)	176 (9%)	78	1764	110	98	0.446
MLS	0.71 (0.66–0.76)	190 (9%)	277 (14%)	173	1756	17	104	0.000
Cisternal compression	0.62 (0.56–0.68)	236 (12%)	161 (8%)	129	1784	105	32	0.000

Kappa values for a positive and negative CT scan (CT+, CT–; see Methods section) and 7 different CT characteristics. Frequencies in which CT characteristics were reported by the investigator sites and by the central review are also shown, with associated McNemar's tests for discordance of paired values.

+/+ (concordant present between central review and site)
–/– (concordant absent between central review and site)
+/– (discordant present central review and absent site)
–/+ (discordant absent central review and present site).
CT, computed tomography; CI, confidence interval; tSAH, traumatic subarachnoid hemorrhage; TAI, traumatic axonal injury; MLS, midline shift.

proportion of discordant findings.[17] We chose a *p* value threshold of 0.05 to indicate systematic differences between the proportion of abnormal findings. Finally, descriptive statistics were used to quantify the variability in the pool of local readers.

All statistical analyses were performed in R (version 3.3.1.).

Results

Agreement between central and local assessments

Table 1 shows the number of times individual CT characteristics were reported by the centers and by the central review for 2050 patients. Good agreement ($\kappa = 0.73$) was found between the central review and the centers for detecting a positive CT (CT+) scan. For most individual CT characteristics, we found relatively good kappa values ($\kappa = 0.62$ to $\kappa = 0.71$), except for TAI lesions ($\kappa = 0.37$). Overall, central reviewers reported more tSAH (45% vs. 38%) and cisternal compression (12% vs. 8%), while investigators reported more contusions (34% vs. 30%) and MLS (14% vs. 9%). Despite good kappa values, these discordances in reporting were significant, as indicated by a positive McNemar's test ($p = 0.000$, 95% CI).

Agreement between central reviewers

Table 2 shows Fleiss kappa values between central reviewers for 100 patients and intra-observer agreement for the three reviewers on a subset of 20 patients. CT+ was almost perfect ($\kappa = 0.96$). For individual CT characteristics, values ranged from substantial to excellent (i.e., epidural hematoma, $\kappa = 0.78$; subdural hematoma,

Table 2. Interobserver and Intra-Observer Agreement between Central Reviewers

	Central inter-observer agreement (n = *100*)	*Detection frequency* (n = *100*)			*Central intra-observer agreement* (n = *20*)		
	Kappa (95% CI)				*Kappa (95% CI)*		
	CR1 + 2 + 3	CR1	CR2	CR3	CR1	CR2	CR3
CT+	0.96 (0.84, 1.07)	61 (61%)	62 (62%)	59 (59%)	1.00 (1.00–1.00)	0.89 (0.67–1.00)	1.00 (1.00–1.00)
CT–	0.96 (0.84, 1.07)	39 (39%)	38 (38%)	41 (41%)	1.00 (1.00–1.00)	0.89 (0.67–1.00)	1.00 (1.00–1.00)
Epidural hematoma	0.78 (0.67, 0.90)	17 (17%)	17 (17%)	16 (16%)	0.32 (–0.27–0.90)	0.62 (0.15–1.00)	0.61 (0.11–1.00)
Acute subdural hematoma	0.81 (0.70, 0.93)	38 (38%)	40 (40%)	34 (34%)	0.80 (0.54–1.00)	0.80 (0.54–1.00)	0.90 (0.71–1.00)
tSAH	0.83 (0.71, 0.94)	49 (49%)	51 (51%)	49 (49%)	0.70 (0.40–1.00)	0.79 (0.53–1.00)	0.60 (0.26–0.94)
Contusion	0.87 (0.75, 0.98)	34 (34%)	36 (36%)	33 (33%)	0.90 (0.71–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
TAI	0.84 (0.73, 0.95)	12 (12%)	12 (12%)	11 (11%)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
MLS	0.84 (0.73, 0.96)	11 (11%)	11 (11%)	14 (14%)	0.77 (0.35–1.00)	0.83 (0.50–1.00)	0.77 (0.39–1.00)
Cisternal compression	0.73 (0.62, 0.84)	15 (15%)	17 (17%)	22 (22%)	0.69 (0.31–1.00)	0.58 (0.19–0.98)	0.73 (0.39–1.00)

Kappa values for a positive and negative CT scan (CT+, CT–, see Methods) and 7 different CT characteristics. Frequencies are shown in which CT characteristics were reported by the central review for a subset of patients ($n = 100$) and intra-observer agreement is shown for the three protocol-trained central reviewers for 20 patients.

CI, confidence interval; CR, central reader; CT, computed tomography; tSAH, traumatic subarachnoid hemorrhage; TAI, traumatic axonal injury; MLS, midline shift.

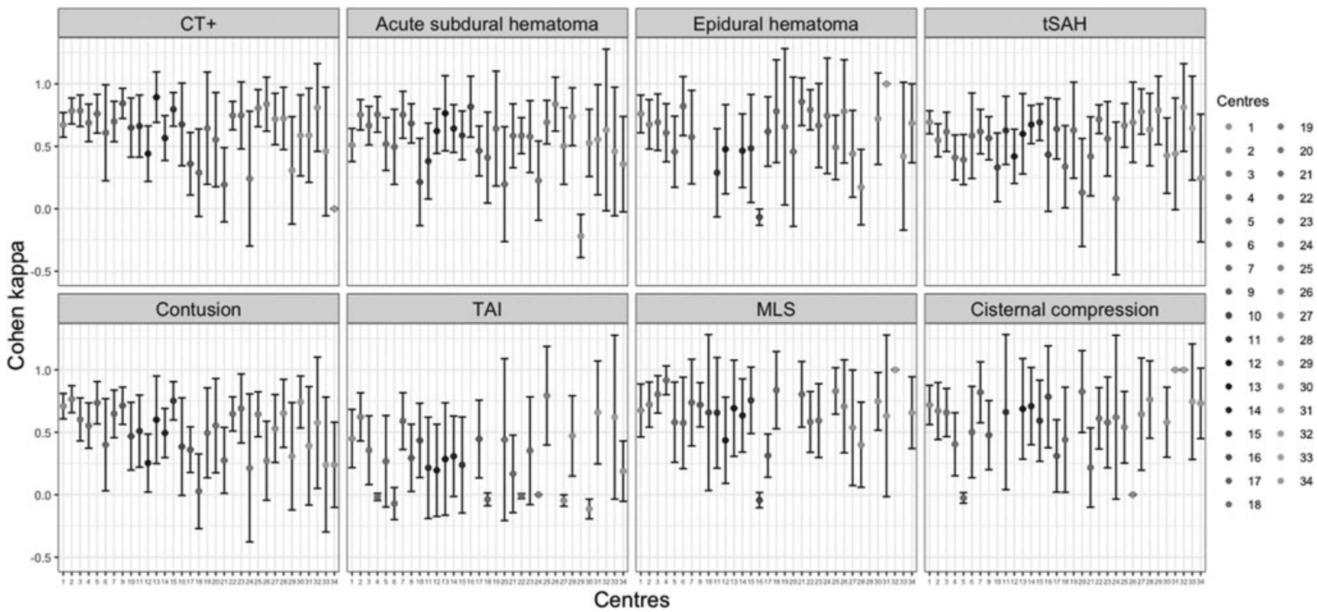

FIG. 1. Variability between centers in agreement with the central review for a positive computed tomography scan (CT+) and seven CT characteristics. The x-axis displays the individual centers and the dots represent the associated kappa value for each center. Substantial variability exists between different centers in how much they agree with the central review.

$\kappa = 0.81$; tSAH, $\kappa = 0.83$; contusion, $\kappa = 0.87$; TAI, $\kappa = 0.84$; cisternal compression, $\kappa = 0.73$; MLS, $\kappa = 0.84$). Intra-observer agreement was excellent for all three reviewers for all CT characteristics, except for epidural hematoma in one reviewer ($\kappa = 0.32$) and cisternal compression in another reviewer ($\kappa = 0.58$)

Variability between centers

Variability between centers in agreement with central review. Figure 1 shows the agreement between the individual centers and the standardized central review for CT+ and for the seven CT characteristics in 2050 patients. The different centers showed substantial variability in how much they agreed with the central review for each individual CT characteristic. Centers that scored poorly on one characteristic did not necessarily do so on all others. No clear trend could be found. Overall however, centers showed highest agreement with the central review for MLS and lowest agreement for TAI.

Variability between centers in amount and background of the readers. The estimated pool of readers at the centers was very large (over 250), with mainly four different medical specialties that performed initial CT assessments (i.e., neurosurgeons, radiologists, intensivists, and radiology residents; Fig. 2A). Radiology residents were included in our analysis because they are crucial in first-line assessment. Years of experience in the case of residents indicates the year of residency. Overall, the level of experience of the readers was highly variable (Fig. 2B). However, the main group of readers were radiologists with over 10 years of experience.

Discussion

To our knowledge, this is the first large-scale study that has systematically compared central with local radiological evaluation of acute CT pathology in TBI. Our data indicate that despite the differences in workflow, the agreement between central reviewers and local centers is good for identifying the presence or absence of structural abnormalities (CT+, CT−). CT positive and CT negative patients can thus accurately be differentiated in both local and centralized radiologic evaluations. This is an important finding for the reliability of research studies that investigate which predictors (e.g., blood-based biomarkers) can differentiate between complicated (CT+) and uncomplicated (CT−) TBI patients.[18–22] Agreement was also relatively good for the evaluation of most individual CT characteristics, specifically for space-occupying extra-axial bleedings (i.e., epidural and subdural hematomas), a finding that also has been reported in previous studies.[23,24]

However, substantial disagreement may arise when more detailed classification of injury is needed, even between expert radiologists.[24,25] In our study, this is reflected in the significant scoring discrepancies that were found between the two approaches for the remaining investigated CT characteristics. Despite good kappa values of agreement, four of seven CT characteristics had a positive McNemar's test, which indicates that different reporting tendencies existed between central and local evaluation. Understanding these discordances is crucial to the advancement of multi-center TBI research.

A possible explanation for these discrepancies is the use of discordant reading criteria and terminology. For example, central readers quantified the degree of tSAH according to NINDS TBI-CDEs practices (trace, moderate, or full) and evaluated more anatomical locations compared with the centers (cortical, basal, tentorial, and interhemispheric vs. basal and/or cortical). This could explain why the central review reported more tSAH. However, detection and grading of tSAH is challenging and has been associated with low observer agreement in the past, even when concordant terminology is used.[24,26]

Central reviewers also showed a tendency to report more basal cistern compression. Evaluation of the basal cisterns is highly subjective and depends on reader background, experience and reading criteria. In addition, different ways to evaluate cisternal compression exist. According to the neurosurgical guidelines of 2006, compression should be evaluated at the level of the midbrain (i.e., the quadrigeminal cistern).[27] However, radiologists assess all

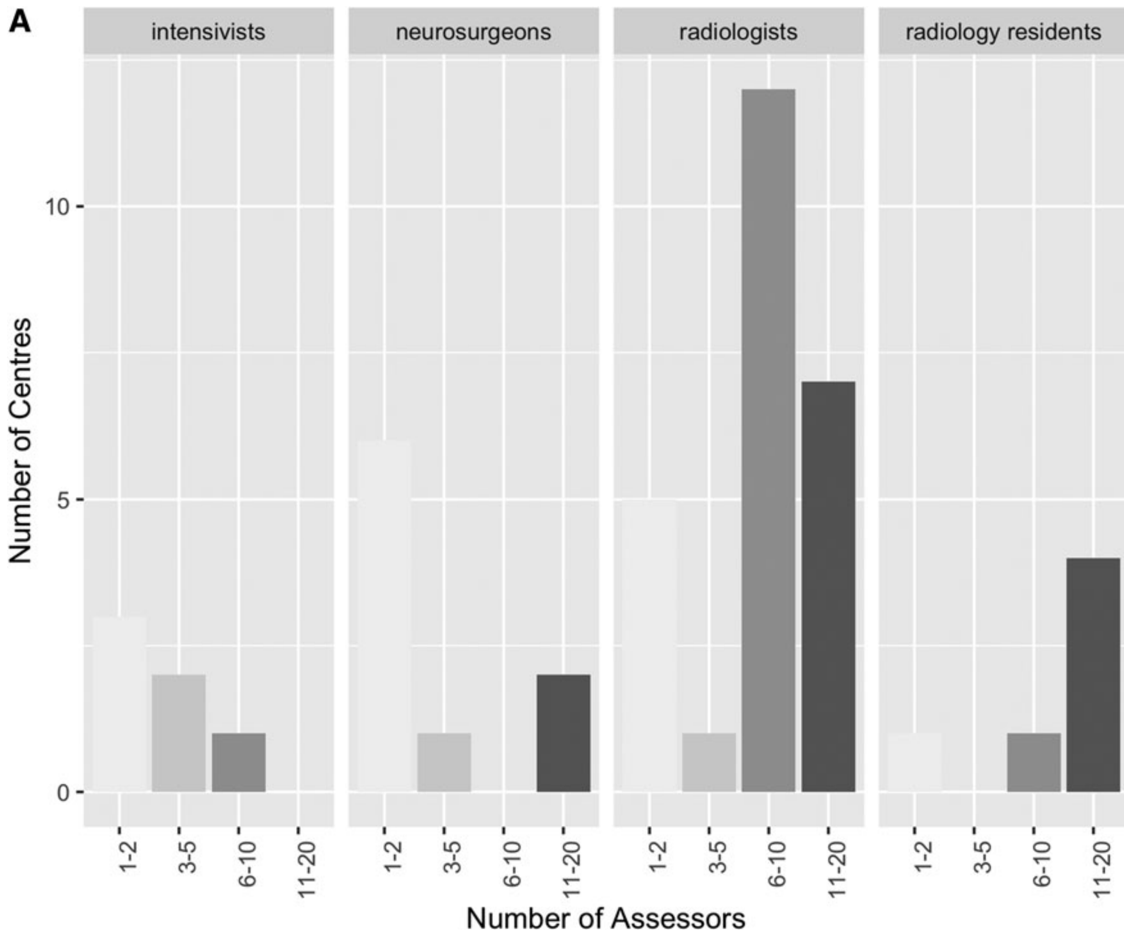

FIG. 2A. Retrospectively collected information about the pool of readers at the level of the center. A substantial number of readers were involved in radiological reading (> 250).

subarachnoid cisterns for any sign of abnormality. In our study, central reviewers also evaluated all cisterns (i.e., the suprasellar, prepontine, quadrigeminal, ambient cistern, and cisterna magna) separately and reported any asymmetry, compression, or effacement according to NINDS TBI-CDE practices (Fig. 3).

Differences in reading criteria and the subjective nature of visual interpretation could explain why central reviewers systematically reported more basal cistern compression.[28] Besides cisternal compression, MLS is an important indicator of mass effect and can help determine the need for surgical intervention.[27] However, depending on local practices and reader background, measurements of this CT characteristic can also vary (Fig. 4). Central readers consistently used one measuring method (Fig. 4, method 2) and only reported shift when greater than 5 mm. In contrast, no strict reading criteria or cut-off values were used at the centers and the pool of readers was very heterogeneous (Fig. 2 and Fig. 3). Retrospective analysis showed that of 104 discordant cases, 93 patients had a shift (89%) that was below 5 mm, indicating that the use of a cut-off value of 5 mm in the central review is most probably the main cause of discordance in our study and not the use of different measuring methods. However, the 11 cases that were genuinely discordant were borderline around 5 mm and differed substantially between the three methods.

Finally, we found significant differences in the classification of contusion and TAI. Small TAI lesions and cortical contusions can be challenging to distinguish on CT, especially when they are occurring at the gray–white matter junction (Fig. 5). Central reviewers reported all focal hyperdense axonal injuries as TAI, including isolated ones that did not span multiple areas of the brain. In contrast, local readers reported diffuse axonal injury (DAI), which could have introduced a reporting bias and a tendency to classify small focal axonal lesions as contusions or only report diffuse lesions as DAI. The fact that local readers reported significantly more contusions supports this hypothesis. The detection of contusions and TAI lesions has been associated with poor observer agreement in the past.[24,25] In addition, as shown in our study, axonal injury terminology is still in a state of flux,[29] which may lead to interpretation differences. Better definitions are therefore needed. At specific locations (i.e., in proximity to the os petrosum), contusions can also easily be missed or overreported due to artefacts, depending on the quality and resolution of the images.[24] Magnetic resonance imaging could offer greater anatomical detail and increased sensitivity for the detection and classification of these two lesion types.[30–32]

For all of the above-described discrepancies, reading criteria, terminology, reader background, and experience play an important role. Central reading in our study was performed by a select panel of only three uniformly trained readers, using strict and standardized reading criteria (NINDS TBI-CDEs) for all of the CT characteristics. Variables were entered directly into the database by the reader who performed the assessment. Excellent interobserver and intra-observer agreement was found between all central readers for

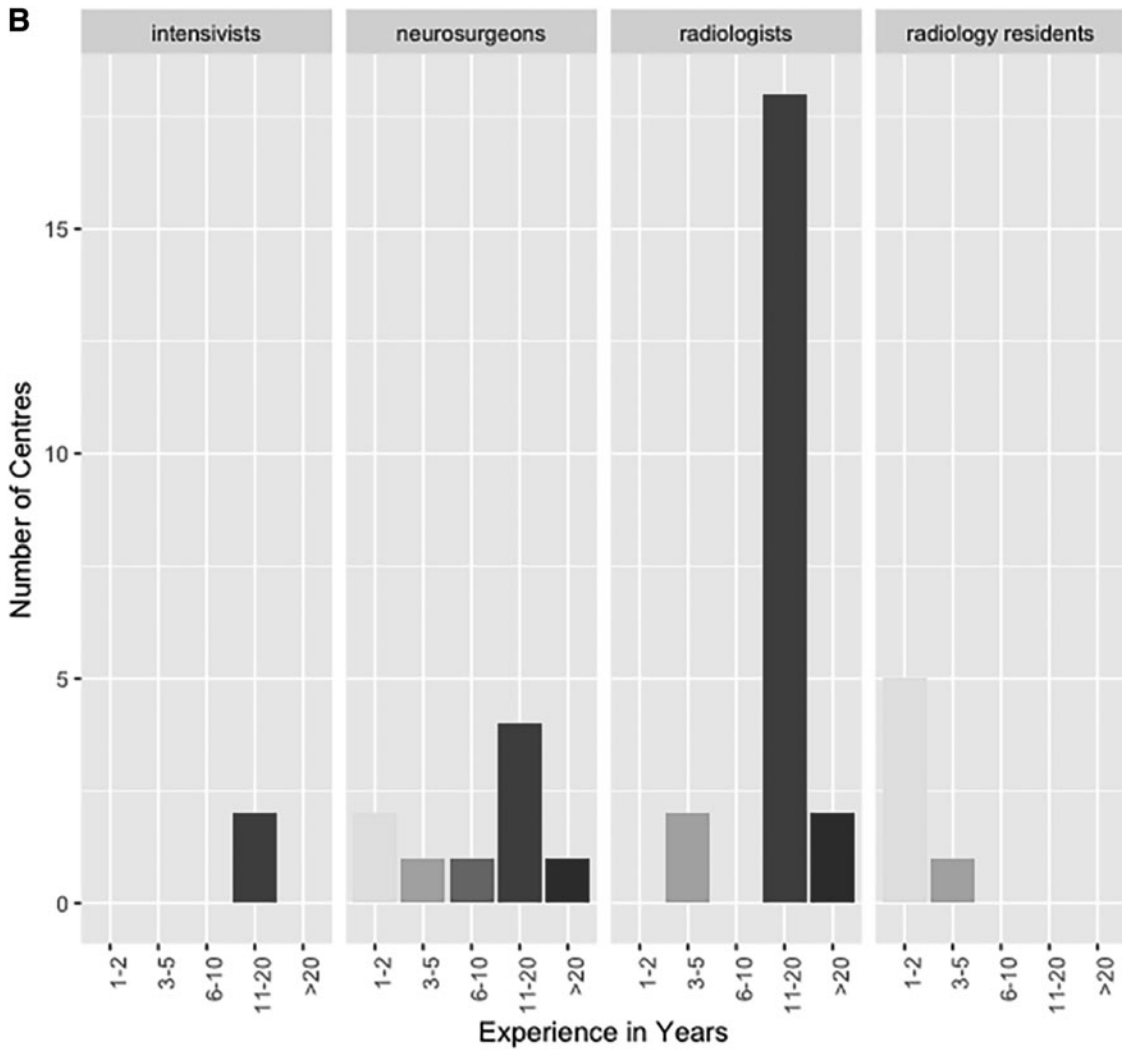

FIG. 2B. Retrospectively collected information about the pool of readers at the level of the center. There was large variability in background and experience between the readers. In most centers the local readers were radiologists with over 10 years of experience.

all of the CT characteristics, including the ones that were discordant with local evaluation. This indicates that no significant differences existed between the assessments of the three reviewers in the central reading panel. It also shows that their individual evaluations were consistent.

The fact that central reading was so consistent allowed us to perform a center-specific analysis to indirectly quantify inter-center differences. This revealed substantial variability between the centers with regard to the extent of agreement with the central review and confirms the existence of great variability in local radiological reading.

Retrospective analysis showed that initial local evaluation of the CT scans was performed by over 250 readers with different backgrounds, different levels of experience and without the use of strict reading criteria. In addition, CT characteristics were not always entered by the physician who performed the assessment. In more than half of the cases, the variables were entered into the database by a third person, based on the radiological report, which could have been an extra source of variability and human error. This approach, however, reflects common procedures in recruiting centers.

It is difficult, if not impossible, to implement strict reading criteria at the level of the centers, where the evaluation is performed in an emergency setting and where time is of the essence. In contrast, in off-site central reading, the readers can go through the structured template without any pressure of time or responsibility to guide therapeutic decision-making. This could be another possible reason why we find reading differences for certain lesion types, especially those that the central reviewers tend to report more of. Our study shows that in large-scale TBI studies, the pool of readers becomes too heterogeneous and substantial variability arises between their radiological readings, which could reduce the reliability and clinical usefulness of the final radiological data. Our study also highlights the importance of using well-defined standardized reading criteria and confirms that an off-site centralized review process using NINDS TBI-CDEs considerably increases reading consistency and reproducibility. The data, generated by central reviewers, are highly reliable, minimize observer variability, and facilitate analyses on large datasets between and across TBI studies. In light of the urgent calls to standardize data collection in TBI research,[33] we therefore strongly recommend the implementation of a central review process in large-scale multi-center TBI studies.

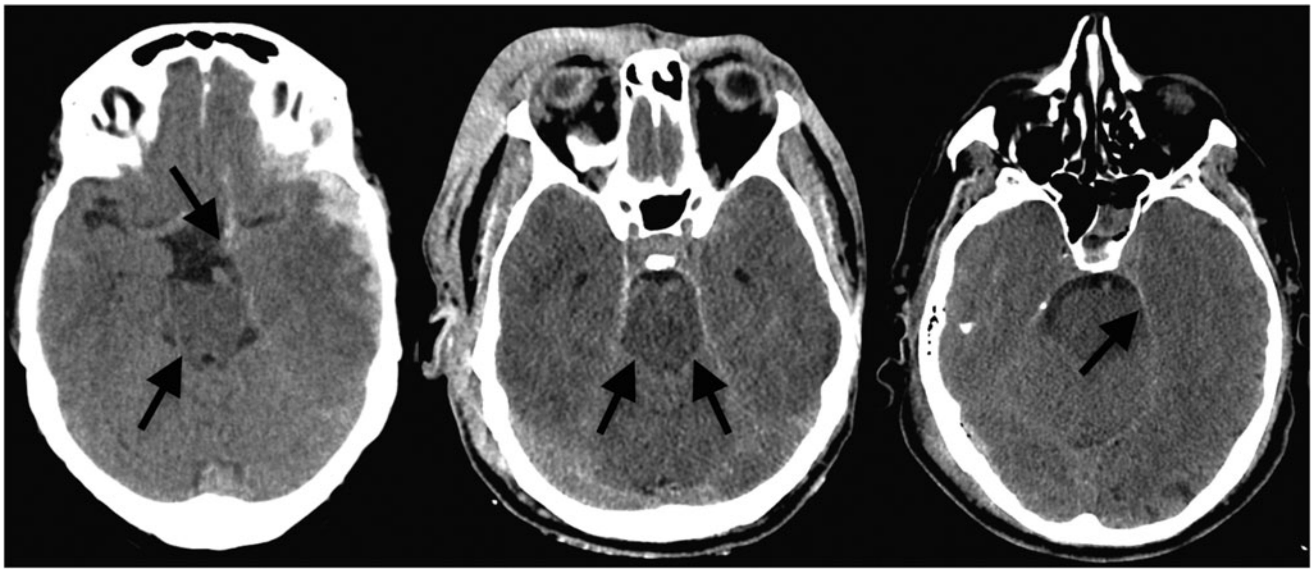

FIG. 3. Examples of discordances in three different patients between the central review and the centers for basal cistern compression. The arrows indicate subarachnoid cisterns that were reported as compressed by the central review, but overall, were considered normal by the centers.

We acknowledge several limitations inherent to our study. First, kappa statistics are influenced by prevalence,[34] which restricted us to select individual centers with a large enough sample to compare with the central review ($n > 10$). For some of these centers, certain CT pathologies did not occur often, which can explain the large confidence intervals in the center-specific analysis. The same holds true for the intra-observer dataset ($n = 20$), where some CT characteristics (e.g., epidural hematoma) occurred less frequently. A second limitation is that we required a retrospective analysis to uncover the number of local readers, their background, and experience. This provided an estimate of how many readers were actually involved and what their level of experience was, as not all centers could retrieve all the requested information. Finally, the lack of other prognostically important CT characteristics in our definition of a CT+ (i.e., skull fractures, pneumocephalus, intraventricular hemorrhage, ventricular compression, brain herniation, etc.) may be considered a limitation. Central reviewers assessed these characteristics, but they were not evaluated at the centers and could therefore not be included in our comparison.

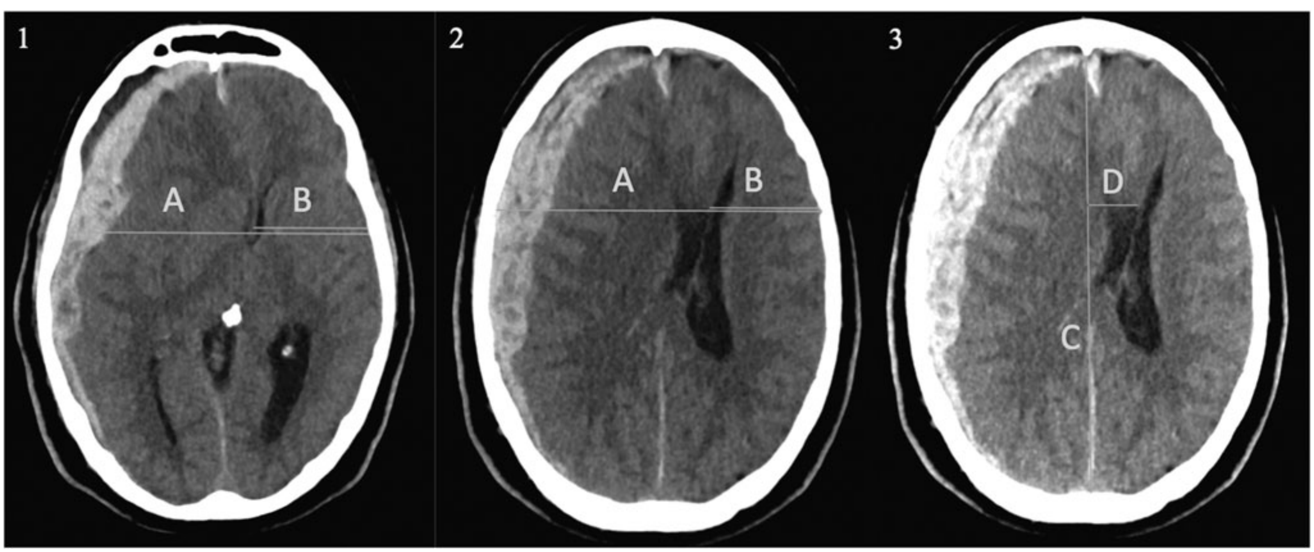

FIG. 4. Different ways to measure midline shift (MLS) in one patient. **(1)** The (A/2-B) method according to Bullock and colleagues,[27] where A is the width of the intracranial space and B is the distance from the tabula interna to the septum pellucidum at the foramen of Monro (MLS = 1.44 cm). **(2)** The (A/2-B) method where shift is measured at the foramen of Monro, or alternatively at the site of largest displacement, according to the Common Data Elements (TBI-CDE) (MLS = 2.01 cm). **(3)** A third method, which is commonly used in routine radiological practice. The ideal midline C is determined as the line between the most anterior and posterior part of the falx cerebri. Line D is drawn to the septum pellucidum and is then calculated as shift (MLS = 1.94 cm).

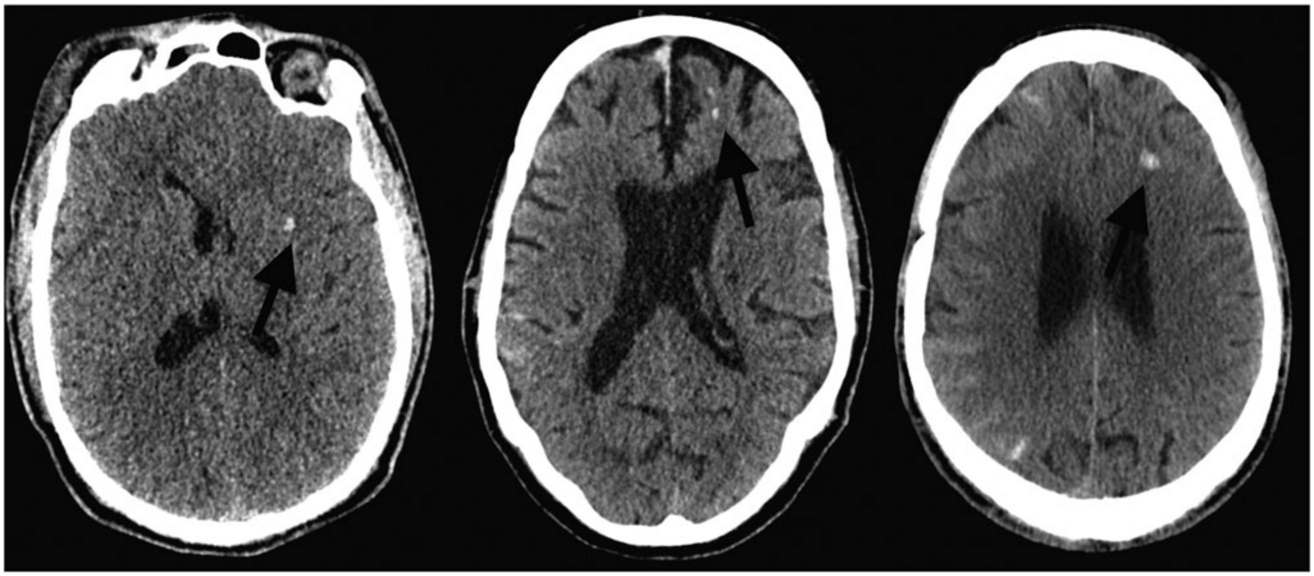

FIG. 5. Examples of discordances in three different patients between the central review and the centers for traumatic axonal injury (TAI). The small focal hyperdense lesions indicated by the arrows were all classified as TAI by the central review, as opposed to contusion by the centers. Lesions occurring at the gray–white matter junction are specifically difficult to discriminate on computed tomography imaging.

Conclusion

Our results indicate good agreement between central reviewers and local investigators for the differentiation between CT positive (CT+) and CT negative (CT−) TBI patients. We also found relatively good agreement for the evaluation of most individual acute CT characteristics, particularly for extra-axial bleedings. However, relevant scoring discrepancies exist between the two approaches upon subclassification of injury and substantial inter-center variability was found in local radiological reading. This is most probably attributable to the large size and heterogeneity of the pool of readers. In contradistinction, interobserver and intra-observer agreement between the select panel of central reviewers was excellent for almost all CT characteristics. We therefore conclude that a standardized central review process with strict reading criteria reduces reader variability, offers a more consistent radiological reading, produces more reproducible data, and should be recommended for implementation in multi-center TBI studies.

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CENTER-TBI Investigators and Participants

Ackerlund, Cecilia,[1] Adams, Hadie,[2] Agnoletti, Vanni,[3] Allanson, Judith,[4] Amrein, Krisztina,[5] Andaluz, Norberto,[6] Andelic, Nada,[7] Andreassen, Lasse,[8] Antun, Azasevac,[9] Anke, Audny,[10] Antoni, Anna,[11] Ardon, Hilko,[12] Audibert, Gérard,[13] Auslands, Kaspars,[14] Azouvi, Philippe,[15] Azzolini, Maria Luisa,[16] Baciu, Camelia,[17] Badenes, Rafael,[18] Bartels, Ronald,[19] Barzó, Pál,[20] Bauerfeind, Ursula,[21] Beauvais, Romuald,[22] Beer, Ronny,[23] Belda, Francisco Javier,[18] Bellander, Bo-Michael,[24] Belli, Antonio,[25] Bellier, Rémy,[26] Benali, Habib,[27] Benard, Thierry,[26] Berardino, Maurizio,[28] Beretta, Luigi,[16] Beynon, Christopher,[29] Bilotta, Federico,[18] Binder, Harald,[11] Biqiri, Erta,[17] Blaabjerg, Morten,[30] den Boogert, Hugo,[19] Bouzat, Pierre,[31] Bragge, Peter,[32] Brazinova, Alexandra,[33] Brinck, Vibeke,[34] Brooker, Joanne,[35] Brorsson, Camilla,[36] Buki, Andras,[37] Bullinger, Monika,[38] Calappi, Emiliana,[39] Calvi, Maria Rosa,[16] Cameron, Peter,[40] Carbayo Lozano, Guillermo,[41] Carbonara, Marco,[39] Carise, Elsa,[26] Carpenter, K.,[42] Castaño-León, Ana M.,[43] Causin, Francesco,[44] Chevallard, Giorgio,[17] Chieregato, Arturo,[17] Citerio, Giuseppe,[45,46] Cnossen, Maryse,[47] Coburn, Mark,[48] Coles, Jonathan,[49] Coles-Kemp, Lizzie,[50] Collett, Johnny,[50] Cooper, Jamie D.,[51] Correia, Marta,[52] Covic, Amra,[53] Curry, Nicola,[54] Czeiter, Endre,[55] Czosnyka, Marek,[56] Dahyot-Fizelier, Claire,[26] Damas, François,[57] Damas, Pierre,[58] Dawes, Helen,[59] De Keyser, Véronique,[60] Della Corte, Francesco,[61] Depreitere, Bart,[62] de Ruiter, Godard C.W.,[63] Dilvesi, Dula,[9] Ding, Shenghao,[64] Dippel, Diederik,[65] Dixit, Abhishek,[66] Donoghue, Emma,[40] Dreier, Jens,[67] Dulière, Guy-Loup,[57] Eapen, George,[68] Engemann, Heiko,[53] Ercole, Ari,[66] Esser, Patrick,[59] Ezer, Erzsébet,[69] Fabricius, Martin,[70] Feigin, Valery L.,[71] Feng, Junfeng,[64] Foks, Kelly,[65] Fossi, Francesca,[17] Francony, Gilles,[31] Freo, Ulderico,[72] Frisvold, Shirin,[73] Furmanov, Alex,[74] Gagliardo, Pablo,[75] Galanaud, Damien,[27] Gantner, Dashiell,[40] Gao, Guoyi,[76] Geleijns, Karin,[42] George, Pradeep,[1] Ghuysen, Alexandre,[77] Giga, Lelde,[78] Giraud, Benoit,[26] Glocker, Ben,[79] Golubovic, Jagos, [9] Gomez, Pedro A.,[43] Grossi, Francesca,[61] Gruen, Russell L.,[80] Gupta, Deepak,[81] Haagsma, Juanita A.,[47] Haitsma, Iain,[82] Hartings, Jed A.,[83] Helbok, Raimund,[23] Helseth, Eirik,[84] Hertle, Daniel,[30] Hoedemaekers, Astrid,[85] Hoefer, Stefan,[53] Horton, Lindsay,[86] Huijben, Jilske,[47] Hutchinson, Peter J.,[2] Håberg Asta, Kristine,[87] Jacobs, Bram,[88] Jankowski, Stefan,[68] Jarrett, Mike,[34] Jelaca, Bojan,[9] Jiang, Ji-yao,[76] Jones, Kelly,[89] Kamnitsas, Konstantinos,[79] Karan, Mladen,[6] Katila Ari,[90] Kaukonen, Maija,[91] Kerforne, Thomas,[26] Kivisaari, Riku,[91] Kolias, Angelos G.[2] Kolumbán, Bálint,[92] Kompanje, Erwin,[93] Kolundzija, Ksenija,[94] Kondziella,

Daniel,[70] Koskinen, Lars-Owe,[36] Kovács, Noémi,[92] Lagares, Alfonso,[43] Lanyon, Linda,[1] Laureys, Steven,[95] Lecky, Fiona,[96] Ledig, Christian,[79] Lefering, Rolf,[97] Legrand,Valerie,[98] Lei, Jin,[64] Levi, Leon,[99] Lightfoot, Roger,[100] Lingsma, Hester,[47] Loeckx, Dirk,[101] Lozano, Angels,[18] MacDonald, Stephen,[102] Maegele, Marc,[103] Majdan, Marek,[33] Major, Sebastian,[104] Manara, Alex,[105] Manley, Geoffrey,[106] Martin, Didier[1,07] Martino, Costanza,[3] Maruenda, Armando,[18] Maréchal, Hugues,[57] Masala, Alessandro,[3] Mattern, Julia,[29] McFadyen, Charles,[66] McMahon, Catherine,[108] Melegh, Béla,[109] Menon, David,[66] Menovsky, Tomas,[60] Morganti-Kossmann, Cristina,[110] Mulazzi, Davide,[39] Muraleedharan, Visakh,[1] Murray, Lynnette,[40] Mühlan, Holger,[111] Nair, Nandesh,[60] Negru, Ancuta,[112] Nelson, David,[1] Newcombe, Virginia,[66] Nieboer, Daan,[47] Noirhomme, Quentin,[95] Nyirádi, József,[5] Oddo, Mauro,[113] Oldenbeuving, Annemarie,[114] Oresic, Matej,[115] Ortolano, Fabrizio,[39] Palotie, Aarno,[116,117,118] Patruno, Adriana,[120] Payen, Jean-François,[31] Perera, Natascha,[22] Perlbarg, Vincent,[27] Persona, Paolo,[121] Peul, Wilco,[63] Piippo-Karjalainen, Anna,[91] Pili Floury, Sébastien,[122] Pirinen, Matti,[116] Ples, Horia,[112] Poca, Maria Antonia,[123] Polinder, Suzanne,[47] Pomposo, Inigo,[41] Posti, Jussi,[90] Puybasset, Louis,[124] Radoi, Andreea,[123] Ragauskas, Arminas,[125] Raj, Rahul,[91] Rambadagalla, Malinka,[126] Real, Ruben,[53] Rehorčíková, Veronika,[33] Rhodes, Jonathan,[127] Ripatti, Samuli,[116] Rocka, Saulius,[125] Roe, Cecilie,[128] Roise, Olav,[129] Roks, Gerwin,[130] Rosand, Jonathan,[131] Rosenfeld, Jeffrey,[110] Rosenlund, Christina,[132] Rosenthal, Guy,[74] Rossaint, Rolf,[48] Rossi, Sandra,[121] Rueckert, Daniel,[79] Rusnák, Martin,[133] Sacchi, Marco,[17] Sahakian, Barbara,[66] Sahuquillo, Juan,[123] Sakowitz, Oliver,[134,135] Sala, Francesca,[120] Sanchez-Porras, Renan,[134] Sandor, Janos,[136] Santos, Edgar,[29] Sasu, Luminita,[61] Savo, Davide,[120] Schäffer, Nadin,[103] Schipper, Inger,[137] Schlößer, Barbara,[21] Schmidt, Silke,[111] Schoechl, Herbert,[138] Schoonman, Guus,[130] Schou, Rico Frederik,[139] Schwendenwein, Elisabeth,[11] Schöll, Michael,[29] Sir, Özcan,[140] Skandsen, Toril,[141] Smakman, Lidwien,[63] Smeets, Dirk,[101] Smielewski, Peter,[56] Sorinola, Abayomi,[142] Stamatakis, Emmanuel,[66] Stanworth, Simon,[54] Steinbüchel, Nicole,[143] Stevanovic, Ana,[48] Stevens, Robert,[144] Stewart, William,[145] Steyerberg, Ewout W.,[47,146] Stocchetti, Nino,[147] Sundström, Nina,[36] Synnot, Anneliese,[34,148] Taccone, Fabio Silvio,[18] Takala, Riikka,[90] Tamás, Viktória,[142] Tanskanen, Päivi,[91] Taylor, Mark Steven,[33] Te Ao, Braden,[71] Tenovuo, Olli,[90] Telgmann, Ralph,[53] Teodorani, Guido,[149] Theadom, Alice,[71] Thomas, Matt,[105] Tibboel, Dick,[42] Tolias, Christos,[150] Tshibanda, Jean-Flory Luaba,[151] Trapani, Tony,[40] Tudora, Cristina Maria,[112] Vajkoczy, Peter,[67] Vallance, Shirley,[43] Valeinis, Egils,[78] Van der Steen, Gregory,[60] van der Jagt, Mathieu,[152] van der Naalt, Joukje,[88] van Dijck, Jeroen T.J.M.,[63] van Essen, Thomas A.,[63] Van Hecke, Wim,[101] van Heugten, Caroline,[59] Van Praag, Dominique,[60] Van Waesberghe, Julia,[48] Vanhaudenhuyse, Audrey,[27,95] Vargiolu, Alessia,[120] Vega, Emmanuel,[153] Velt, Kimberley,[47] Vespa, Paul M.,[154] Vik, Anne,[155] Vilcinis, Rimantas,[156] Vizzino, Giacinta,[17] Vleggeert-Lankamp, Carmen,[63] Volovici, Victor,[82] Voormolen, Daphne,[47] Vulekovic, Peter,[9] Vámos, Zoltán,[69] Wade, Derick,[59] Wang, Kevin K.W.,[157] Wang, Lei,[64] Wessels, Lars,[158] Wildschut, Eno,[42] Williams, Guy,[66] Wilson, Lindsay,[86] Winkler, Maren K.L.,[104] Wolf, Stefan,[158] Ylén, Peter,[159] Younsi, Alexander,[29] Zaaroor, Menashe,[99] Zhihui, Yang,[160] Ziverte, Agate,[78] Zumbo, Fabrizio.[3]

[1]Karolinska Institutet, INCF International Neuroinformatics Coordinating Facility, Stockholm, Sweden.

[2]Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke's Hospital and University of Cambridge, Cambridge, United Kingdom. United Kingdom.

[3]Department of Anesthesia and Intensive Care, M. Bufalini Hospital, Cesena, Italy.

[4]Department of Clinical Neurosciences, Addenbrooke's Hospital and University of Cambridge, Cambridge, United Kingdom.

[5]János Szentágothai Research Centre, University of Pécs, Pécs, Hungary.

[6]University of Cincinnati, Cincinnati, Ohio.

[7]Division of Surgery and Clinical Neuroscience, Department of Physical Medicine and Rehabilitation, Oslo University Hospital and University of Oslo, Oslo, Norway.

[8]Department of Neurosurgery, University Hospital Northern Norway, Tromso, Norway.

[9]Department of Neurosurgery, Clinical Centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia.

[10]Department of Physical Medicine and Rehabilitation, University Hospital, Northern Norway.

[11]Trauma Surgery, Medical University Vienna, Vienna, Austria.

[12]Department of Neurosurgery, Elisabeth-Tweesteden Ziekenhuis, Tilburg, the Netherlands.

[13]Department of Anesthesiology and Intensive Care, University Hospital Nancy, Nancy, France.

[14]Riga Eastern Clinical University Hospital, Riga, Latvia.

[15]Raymond Poincare hospital, Assistance Publique—Hopitaux de Paris, Paris, France.

[16]Department of Anesthesiology and Intensive Care, San Raffaele University Hospital, Milan, Italy.

[17]NeuroIntensive Care, Niguarda Hospital, Milan, Italy.

[18]Department Anesthesiology and Surgical-Trauma Intensive Care, Hospital Clinic Universitari de Valencia, Spain.

[19]Department of Neurosurgery, Radboud University Medical Center, Nijmegen, the Netherlands.

[20]Department of Neurosurgery, University of Szeged, Szeged, Hungary.

[21]Institute for Transfusion Medicine (ITM), Witten/Herdecke University, Cologne, Germany.

[22]International Projects Management, ARTTIC, Munchen, Germany.

[23]Department of Neurology, Neurological Intensive Care Unit, Medical University of Innsbruck, Innsbruck, Austria.

[24]Department of Neurosurgery and Anesthesia and intensive care medicine, Karolinska University Hospital, Stockholm, Sweden.

[25]NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham, U.K

[26]Intensive Care Unit, CHU Poitiers, Poitiers, France.

[27]Anesthesie-Réanimation, Assistance Publique—Hopitaux de Paris, Paris, France.

[28]Department of Anesthesia and ICU, AOU Città della Salute e della Scienza di Torino— Orthopedic and Trauma Center, Torino, Italy.

[29]Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany.

[30]Department of Neurology, Odense University Hospital, Odense, Denmark.

[31]Department of Anesthesiology and Intensive Care, University Hospital of Grenoble, Grenoble, France.

[32]BehaviourWorks Australia, Monash Sustainability Institute, Monash University, Victoria, Australia.

[33]Department of Public Health, Faculty of Health Sciences and Social Work, Trnava University, Trnava, Slovakia.

[34]Quesgen Systems Inc., Burlingame, California.

[35]Australian and New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of

Public Health and Preventive Medicine, Monash University, Melbourne, Australia.
[36]Department of Neurosurgery, Umea University Hospital, Umea, Sweden.
[37]Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program, Pecs, Hungary.
[38]Department of Medical Psychology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany.
[39]Neuro ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.
[40]ANZIC Research Centre, Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Vitoria, Australia.
[41]Department of Neurosurgery, Hospital of Cruces, Bilbao, Spain.
[42]Intensive Care and Department of Pediatric Surgery, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, the Netherlands.
[43]Department of Neurosurgery, Hospital Universitario 12 de Octubre, Madrid, Spain.
[44]Department of Neuroscience, Azienda Ospedaliera Università di Padova, Padova, Italy
[45]NeuroIntensive Care, ASST di Monza, Monza, Italy.
[46]School of Medicine and Surgery, Università Milano Bicocca, Milano, Italy.
[47]Department of Public Health, Erasmus Medical Center-University Medical Center, Rotterdam, the Netherlands.
[48]Department of Anaesthesiology, University Hospital of Aachen, Aachen, Germany.
[49]Department of Anesthesia and Neurointensive Care, Cambridge University Hospital NHS Foundation Trust, Cambridge, United Kingdom.
[50]Movement Science Group, Oxford Institute of Nursing, Midwifery and Allied Health Research, Oxford Brookes University, Oxford, United Kingdom.
[51]School of Public Health and PM, Monash University and The Alfred Hospital, Melbourne, Victoria, Australia.
[52]Radiology/MRI department, MRC Cognition and Brain Sciences Unit, Cambridge, United Kingdom.
[53]Institute of Medical Psychology and Medical Sociology, Universitätsmedizin Göttingen, Göttingen, Germany.
[54]Oxford University Hospitals NHS Trust, Oxford, United Kingdom.
[55]Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program (Grant No. KTIA 13 NAP-A-II/8), Pecs, Hungary.
[56]Brain Physics Lab, Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom.
[57]Intensive Care Unit, CHR Citadelle, Liège, Belgium.
[58]Intensive Care Unit, CHU, Liège, Belgium.
[59]Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, United Kingdom.
[60]Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium.
[61]Department of Anesthesia and Intensive Care, Maggiore Della Carità Hospital, Novara, Italy.
[62]Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium.
[63]Department of Neurosurgery, Leiden University Medical Center, Leiden, the Netherlands. and Department of Neurosurgery, Medical Center Haaglanden, the Hague, the Netherlands.
[64]Department of Neurosurgery, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.
[65]Department of Neurology, Erasmus MC, Rotterdam, the Netherlands.
[66] Division of Anaesthesia, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom.
[67]Neurologie, Neurochirurgie und Psychiatrie, Charité—Universitätsmedizin Berlin, Berlin, Germany.
[68]Neurointensive Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom.
[69]Department of Anaesthesiology and Intensive Therapy, University of Pécs, Pécs, Hungary.
[70]Departments of Neurology, Clinical Neurophysiology and Neuroanesthesiology, Region Hovedstaden Rigshospitalet, Copenhagen, Denmark.
[71]National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand.
[72]Department of Medicine, Azienda Ospedaliera Università di Padova, Padova, Italy.
[73]Department of Anesthesiology and Intensive care, University Hospital Northern Norway, Tromso, Norway.
[74]Department of Neurosurgery, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.
[75]Fundación Instituto Valenciano de Neurorrehabilitación (FIVAN), Valencia, Spain.
[76]Department of Neurosurgery, Shanghai Renji Hospital, Shanghai Jiaotong University/School of Medicine, Shanghai, China.
[77]Emergency Department, CHU, Liège, Belgium.
[78]Pauls Stradins Clinical University Hospital, Riga, Latvia.
[79]Department of Computing, Imperial College London, London, United Kingdom.
[80]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; and Monash University, Australia.
[81]Department of Neurosurgery, Neurosciences Centre and JPN Apex trauma centre, All India Institute of Medical Sciences, New Delhi-110029, India.
[82]Department of Neurosurgery, Erasmus MC, Rotterdam, the Netherlands.
[83]Department of Neurosurgery, University of Cincinnati, Cincinnati, Ohio.
[84]Department of Neurosurgery, Oslo University Hospital, Oslo, Norway.
[85]Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands.
[86]Division of Psychology, University of Stirling, Stirling, United Kingdom.
[87]Department of Medical Imaging, St. Olav's Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.
[88]Department of Neurology, University Medical Center Groningen, Groningen, the Netherlands.
[89]National Institute for Stroke and Applied Neurosciences of the AUT University, Auckland, New Zealand.
[90]Rehabilitation and Brain Trauma, Turku University Central Hospital and University of Turku, Turku, Finland.
[91]Helsinki University Central Hospital, Helsinki, Finland.
[92]Hungarian Brain Research Program—Grant No. KTIA 13 NAP-A-II/8, University of Pécs, Pécs, Hungary.

[93]Department of Intensive Care and Department of Ethics and Philosophy of Medicine, Erasmus Medical Center, Rotterdam, the Netherlands.

[94]Department of Psichiatry, Clinical Centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia.

[95]Cyclotron Research Center, University of Liège, Liège, Belgium.

[96]Emergency Medicine Research in Sheffield, Health Services Research Section, School of Health and Related Research (ScHARR), University of Sheffield, Sheffield, United Kingdom.

[97]Institute of Research in Operative Medicine (IFOM), Witten/Herdecke University, Cologne, Germany.

[98]VP Global Project Management CNS, ICON, Paris, France.

[99]Department of Neurosurgery, Rambam Medical Center, Haifa, Israel.

[100]Department of Anesthesiology and Intensive Care, University Hospitals Southhampton NHS Trust, Southhampton, United Kingdom.

[101]icoMetrix NV, Leuven, Belgium.

[102]Cambridge University Hospitals, Cambridge, United Kingdom.

[103]Cologne-Merheim Medical Center (CMMC), Department of Traumatology, Orthopedic Surgery and Sportmedicine, Witten/Herdecke University, Cologne, Germany.

[104]Centrum für Schlaganfallforschung, Charité—Universitätsmedizin Berlin, Berlin, Germany.

[105]Intensive Care Unit, Southmead Hospital, Bristol, Bristol, United Kingdom.

[106]Department of Neurological Surgery, University of California, San Francisco, California.

[107]Department of Neurosurgery, CHU, Liège, Belgium.

[108]Department of Neurosurgery, The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom.

[109]Department of Medical Genetics, University of Pécs, Pécs, Hungary.

[110]National Trauma Research Institute, The Alfred Hospital, Monash University, Melbourne, Victoria, Australia.

[111]Department Health and Prevention, University Greifswald, Greifswald, Germany.

[112]Department of Neurosurgery, Emergency County Hospital Timisoara, Timisoara, Romania.

[113]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

[114]Department of Intensive Care, Elisabeth-Tweesteden Ziekenhuis, Tilburg, the Netherlands.

[115]Department of Systems Medicine, Steno Diabetes Center, Gentofte, Denmark.

[116]Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland.

[117]Analytic and Translational Genetics Unit, Department of Medicine; Psychiatric and Neurodevelopmental Genetics Unit, Department of Psychiatry; Department of Neurology, Massachusetts General Hospital, Boston, MA.

[118]Program in Medical and Population Genetics; The Stanley Center for Psychiatric Research, The Broad Institute of MIT and Harvard, Cambridge, MA.

[119]Department of Radiology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium.

[120]NeuroIntenisve Care Unit, Department of Anesthesia and Intensive Care, ASST di Monza, Monza, Italy.

[121]Department of Anesthesia and Intensive Care, Azienda Ospedaliera Università di Padova, Padova, Italy.

[122]Intensive Care Unit, CHRU de Besançon, Besançon, France.

[123]Department of Neurosurgery, Vall d'Hebron University Hospital, Barcelona, Spain.

[124]Department of Anesthesiology and Critical Care, Pitié - Salpêtrière Teaching Hospital, Assistance Publique, Hôpitaux de Paris and University Pierre et Marie Curie, Paris, France.

[125]Department of Neurosurgery, Kaunas University of technology and Vilnius University, Vilnius, Lithuania

[126]Rezekne Hospital, Latvia.

[127]Department of Anaesthesia, Critical Care and Pain Medicine NHS Lothian and University of Edinburg, Edinburgh, United Kingdom.

[128]Department of Physical Medicine and Rehabilitation, Oslo University Hospital/University of Oslo, Oslo, Norway.

[129]Division of Surgery and Clinical Neuroscience, Oslo University Hospital, Oslo, Norway.

[130]Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands.

[131]Broad Institute, Cambridge MA Harvard Medical School, Boston MA, Massachusetts General Hospital, Boston, MA.

[132]Department of Neurosurgery, Odense University Hospital, Odense, Denmark.

[133]International Neurotrauma Research Organisation, Vienna, Austria.

[134]Klinik für Neurochirurgie, Klinikum Ludwigsburg, Ludwigsburg, Germany.

[135]University Hospital Heidelberg, Heidelberg, Germany.

[136]Division of Biostatistics and Epidemiology, Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary.

[137]Department of Traumasurgery, Leiden University Medical Center, Leiden, the Netherlands.

[138]Department of Anaesthesiology and Intensive Care, AUVA Trauma Hospital, Salzburg, Austria.

[139]Department of Neuroanesthesia and Neurointensive Care, Odense University Hospital, Odense, Denmark.

[140]Department of Emergency Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands.

[141]Department of Physical Medicine and Rehabilitation, St. Olav's Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.

[142]Department of Neurosurgery, University of Pécs, Pécs, Hungary.

[143]Universitätsmedizin Göttingen, Göttingen, Germany.

[144]Division of Neuroscience Critical Care, John Hopkins University School of Medicine, Baltimore, MD.

[145]Department of Neuropathology, Queen Elizabeth University Hospital and University of Glasgow, Glasgow, United Kingdom.

[146]Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands.

[147]Department of Pathophysiology and Transplantation, Milan University, and Neuroscience ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy.

[148]Cochrane Consumers and Communication Review Group, Centre for Health Communication and Participation, School of Psychology and Public Health, La Trobe University, Melbourne, Australia.

[149]Department of Reahabilitation, M. Bufalini Hospital, Cesena, Italy.

[150]Department of Neurosurgery, King's College London, London, United Kingdom.

[151]Radiology/MRI Department, CHU, Liège, Belgium.

[152]Department of Intensive Care, Erasmus MC, Rotterdam, the Netherlands.

[153]Department of Anesthesiology-Intensive Care, Lille University Hospital, Lille, France.

[154]Director of Neurocritical Care, University of California, Los Angeles.

[155]Department of Neurosurgery, St. Olav's Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.

[156]Department of Neurosurgery, Kaunas University of Health Sciences, Kaunas, Lithuania.

[157]Department of Psychiatry, University of Florida, Gainesville, FL.

[158]Interdisciplinary Neuro Intensive Care Unit, Charité—Universitätsmedizin Berlin, Berlin, Germany.

[159]VTT Technical Research Centre, Tampere, Finland.

[160]University of Florida, Gainesville, FL.

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Address correspondence to:
Thijs Vande Vyvere, MSc
Poelsnepstraat 11
9000 Ghent
Belgium

E-mail: thijs.vandevyvere@uantwerpen.be